10019049

(FILE 'HOME' ENTERED AT 13:05:19 ON 28 JUN 2005)

FILE 'CAPLUS' ENTERED AT 13:06:06 ON 28 JUN 2005

L1	186	S	PAROXETINE (2A) HYDROCHLORIDE
L2	46	S	PAROXETINE (2A) HCL
L3	192	S	L1 OR L2
L4	568116	S	MELT OR FUSION
L5	6	S	L3 AND L4
L6	608	S	MOLECULAR DISPERSION
L7	33	S	L6 AND L4
L8	0	S	L7 AND L3
L9	338778	S	DISPERSION
L10	10	S	L3 AND L9
L11	1	S	L10 AND L4

Blessing

10019049

L5 ANSWER 4 OF 6 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1999:42579 CAPLUS
DOCUMENT NUMBER: 130:86197
TITLE: Novel process for manufacturing paroxetine solid dispersions
INVENTOR(S): Krape, Philip J.; Chang, Sou-chan; Hein, William A., II; Teleha, Christopher A.
PATENT ASSIGNEE(S): Endo Pharmaceuticals Inc., USA
SOURCE: PCT Int. Appl., 32 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9900131	A1	19990107	WO 1998-US13350	19980626
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, GW, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
US 5955475	A	19990921	US 1997-885068	19970630
ZA 9805488	A	19990422	ZA 1998-5488	19980624
AU 9881717	A1	19990119	AU 1998-81717	19980626
AU 733194	B2	20010510		
EP 991408	A1	20000412	EP 1998-931648	19980626
EP 991408	B1	20050309		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
BR 9810231	A	20000808	BR 1998-10231	19980626
TR 9903315	T2	20000921	TR 1999-9903315	19980626
NZ 502062	A	20011026	NZ 1998-502062	19980626
JP 2002514227	T2	20020514	JP 1999-509825	19980626
RU 2185820	C2	20020727	RU 2000-102637	19980626
CN 1121219	B	20030917	CN 1998-807966	19980626
CA 2295752	C	20041026	CA 1998-2295752	19980626
CA 2295752	AA	19990107		
AT 290381	E	20050315	AT 1998-931648	19980626
NO 9906484	A	20000225	NO 1999-6484	19991227
HK 1029529	A1	20040102	HK 2001-100318	20010112

PRIORITY APPLN. INFO.:	US 1997-885068	A	19970630
	WO 1998-US13350	W	19980626

AB Solid dispersions of poorly soluble drugs are disclosed which are prepared using a solvent or **fusion** process. Such dispersions are manufactured with the free base of the drug, specifically paroxetine free base. Paroxetine free base and PEG-8000 were mixed and a stream of HCl gas was introduced to the mixture The solidified product was collected and 1H-NMR anal. showed the product was a mixture of PEG and **paroxetine** ·**HCl**. A tablet containing 22.21 mg **paroxetine** ·**HCl** was formulated.

REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

AB Solid dispersions of poorly soluble drugs are disclosed which are prepared

Blessing

using a solvent or **fusion** process. Such dispersions are manufactured with the free base of the drug, specifically paroxetine free base. Paroxetine free base and PEG-8000 were mixed and a stream of HCl gas was introduced to the mixture The solidified product was collected and 1H-NMR anal. showed the product was a mixture of PEG and **paroxetine** ·**HCl**. A tablet containing 22.21 mg **paroxetine** ·**HCl** was formulated.

IT Mental disorder
(depression, treatment of; manufacture of paroxetine solid dispersions using solvents or **fusion** process)

IT Polyoxyalkylenes, uses
RL: MOA (Modifier or additive use); USES (Uses)
(manufacture of paroxetine solid dispersions using solvents or **fusion** process)

IT Drug delivery systems
(tablets; manufacture of paroxetine solid dispersions using solvents or **fusion** process)

IT 9003-11-6, Ethylene glycol-propylene glycol copolymer 9003-39-8, PVP 9004-64-2, Hydroxypropyl cellulose 9004-65-3, Hydroxypropyl methyl cellulose 9004-67-5, Methyl cellulose 25322-68-3, Polyethylene glycol
RL: MOA (Modifier or additive use); USES (Uses)
(manufacture of paroxetine solid dispersions using solvents or **fusion** process)

IT 64-17-5, Ethanol, uses 67-56-1, Methanol, uses 67-63-0, Isopropanol, uses 71-23-8, Propanol, uses 71-36-3, Butanol, uses 78-83-1, Isobutanol, uses 78-92-2, sec-Butanol
RL: NUU (Other use, unclassified); USES (Uses)
(manufacture of paroxetine solid dispersions using solvents or **fusion** process)

IT 61869-08-7, Paroxetine
RL: PEP (Physical, engineering or chemical process); PROC (Process)
(manufacture of paroxetine solid dispersions using solvents or **fusion** process)

IT 78246-49-8P, **Paroxetine hydrochloride**
RL: PNU (Preparation, unclassified); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(manufacture of **paroxetine** solid dispersions using solvents or **fusion** proce

10019049

L5 ANSWER 5 OF 6 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1996:705783 CAPLUS
DOCUMENT NUMBER: 125:339069
TITLE: Homogeneous mixtures of low temperature-melting drugs and additives for controlled release
INVENTOR(S): Cheskin, Howard; Hale, Thomas J.; Van Scoik, Kurt G.; Zhou, Ji
PATENT ASSIGNEE(S): Abbott Laboratories, USA
SOURCE: PCT Int. Appl., 23 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9631197	A1	19961010	WO 1996-US4513	19960402
W: CA, JP, MX				
RW: AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
CA 2216934	AA	19961010	CA 1996-2216934	19960402
EP 818990	A1	19980121	EP 1996-910705	19960402
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, PT, IE, FI				
JP 11503163	T2	19990323	JP 1996-530428	19960402
US 5807574	A	19980915	US 1997-879468	19970620
PRIORITY APPLN. INFO.:			US 1995-415401 A	19950403
			WO 1996-US4513 W	19960402

AB Disclosed herein is a controlled-release formulation comprising, in combination a therapeutically-effective dosage of drug which **melts** at low temperature and an additive selected from the group consisting of Et cellulose, Me cellulose, hydroxypropyl cellulose, polyacrylamide, ethylene-vinyl acetate copolymer, poly(Me methacrylate), polyhydroxyethyl methacrylate and waxes, and the like, such that the additive and the drug form a homogeneous drug-additive composite, wherein the drug is selected from the group consisting of: divalproex sodium (I), ibuprofen, ramipril, dibenzyline, erythrityl tetranitrate, isosorbide dinitrate, methsuximide, ketoprofen, gemfibrozil, **paroxetine·HCl**, and trimipramine maleate. I 25 g were melted with 1.25 g of polyethylene wax at 115° and the resulting molten composite was filled into capsules, which were subjected to USP dissoln. test in simulated gastric fluid. The capsules showed controlled release of I such that only .apprx.60 % of the I in the composite was released over 24 h.

AB Disclosed herein is a controlled-release formulation comprising, in combination a therapeutically-effective dosage of drug which **melts** at low temperature and an additive selected from the group consisting of Et cellulose, Me cellulose, hydroxypropyl cellulose, polyacrylamide, ethylene-vinyl acetate copolymer, poly(Me methacrylate), polyhydroxyethyl methacrylate and waxes, and the like, such that the additive and the drug form a homogeneous drug-additive composite, wherein the drug is selected from the group consisting of: divalproex sodium (I), ibuprofen, ramipril, dibenzyline, erythrityl tetranitrate, isosorbide dinitrate, methsuximide, ketoprofen, gemfibrozil, **paroxetine·HCl**, and trimipramine maleate. I 25 g were melted with 1.25 g of polyethylene wax at 115° and the resulting molten composite was filled into capsules, which were subjected to USP dissoln. test in simulated gastric fluid. The capsules showed controlled release of I such that only .apprx.60 % of the I in the composite was released over 24 h.

IT 59-96-1, Dibenzyline 77-41-8, Methsuximide 87-33-2, Isosorbide

dinitrate 521-78-8, Trimipramine maleate 7297-25-8, Erythrityl tetranitrate 9003-05-8, Polyacrylamide 9004-57-3, Ethyl cellulose 9004-64-2, Hydroxypropyl cellulose 9004-67-5, Methyl cellulose 9011-14-7, Polymethylmethacrylate 15687-27-1, Ibuprofen 22071-15-4, Ketoprofen 24937-78-8, Ethylene-vinyl acetate copolymer 25249-16-5 25812-30-0, Gemfibrozil 76584-70-8, Divalproex sodium 78246-49-8, **Paroxetine hydrochloride** 87333-19-5, Ramipril
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(homogeneous mixts. of low temperature-melting drugs and additives for controlled release)

10019049

L5 ANSWER 6 OF 6 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1988:192668 CAPLUS
DOCUMENT NUMBER: 108:192668
TITLE: Solid-state forms of **paroxetine hydrochloride**
AUTHOR(S): Buxton, P. Christopher; Lynch, Ian R.; Roe, John M.
CORPORATE SOURCE: Biosci. Res. Cent., Beecham Pharm., Epsom Surrey, KT18 5XQ, UK
SOURCE: International Journal of Pharmaceutics (1988), 42(1-3), 135-43
CODEN: IJPHDE; ISSN: 0378-5173
DOCUMENT TYPE: Journal
LANGUAGE: English
AB **Paroxetine-HCl** (I) exists in two solid state forms differentiated by their degrees of hydration. Form I is a non-hygroscopic hemihydrate and is thermodynamically the more stable. Form II is a hygroscopic anhydrate the moisture content of which is controlled by the prevailing humidity. Form II converts to Form I, if seed crystals of Form I are present, when exposed to humid conditions or if subjected to compression. The rates of transformation were determined by IR spectroscopy and techniques are described to identify the solid state form in compressed tablets. The transformation follows kinetic models described by diffusion and phase boundary processes and the rate constant (k) is related to temperature by the Arrhenius equation. At constant temperature ln k is related to the reciprocal of the compaction pressure. Thermodn. measurements of free energy (ΔGT) and enthalpy (ΔHT) show the two forms to be energetically similar and measurements of dissoln. indicate that both forms would be expected to be bioequivalent.
TI Solid-state forms of **paroxetine hydrochloride**
AB **Paroxetine-HCl** (I) exists in two solid state forms differentiated by their degrees of hydration. Form I is a non-hygroscopic hemihydrate and is thermodynamically the more stable. Form II is a hygroscopic anhydrate the moisture content of which is controlled by the prevailing humidity. Form II converts to Form I, if seed crystals of Form I are present, when exposed to humid conditions or if subjected to compression. The rates of transformation were determined by IR spectroscopy and techniques are described to identify the solid state form in compressed tablets. The transformation follows kinetic models described by diffusion and phase boundary processes and the rate constant (k) is related to temperature by the Arrhenius equation. At constant temperature ln k is related to the reciprocal of the compaction pressure. Thermodn. measurements of free energy (ΔGT) and enthalpy (ΔHT) show the two forms to be energetically similar and measurements of dissoln. indicate that both forms would be expected to be bioequivalent.
IT Heat of **fusion** and Heat of freezing
Heat of solution
(of paroxetin hydrochloride solid-state forms)
IT Solution rate
(of **paroxetine hydrochloride** solid-state forms)
IT Free energy
(of transition, of **paroxetine hydrochloride** solid-state forms)
IT Compaction
Humidity
(**paroxetine hydrochloride** solid-state forms in relation to)

Blessing

10019049

IT 78246-49-8, **Paroxetine hydrochloride**
RL: PRP (Properties)
(solid-state forms of)

Blessing